wherein the bacteria is *E. coli*.

41. (Amended) A method of vaccinating a human or animal subject against a selected bacteria, comprising:

administering to the subject, replication-crippled, morphologically abnormal cells of the bacteria, prepared by incubating the bacteria in the presence of a morpholino-based antisense oligomer having

(a) from 8 to 40 nucleotide subunits, including a targeting base sequence effective to hybridize to a translation initiation region in an mRNA transcribed from a *secA* gene of the selected bacteria; and

(b) uncharged phosphorous-containing chiral intersubunit linkages, as shown in Figures 2A-2D herein,

wherein the bacteria is *E. coli*.

Remarks

In view of the election of species, enclosed herewith, the claims are amended to recite that the targeted protein is an *E. coli secA* protein. Claims not reading on this embodiment are cancelled without prejudice. Applicants reserve the right to pursue the cancelled subject matter in continuing applications.

In addition, independent claims 1, 17 and 36 have been amended for clarity. The phrase: "8 to 40 nucleotide subunits...including a targeting nucleic acid sequence at least 10 nucleotides in length" is amended to ""10 to 40 nucleotide subunits...". By this amendment, the minimum length of the oligomer is set to 10 subunits, since a length of 8 subunits clearly could not include "a targeting nucleic acid sequence at least 10 nucleotides in length". The language is also amended to clarify that the base-pairing moieties make up the targeting antisense sequence.

Claims 16, 23, and 39 are amended to recite a preferred length of the targeting (complementary) sequence. Support for these amendments is found in the specification at, for example, page 10, lines 18-19 and 34-35.

Entry of this amendment prior to examination is respectfully requested. No new matter is added by any of the amendments.

No further fees are believed necessary with this communication. However, the Commissioner is hereby authorized and requested to charge any deficiency in fees herein, or credit any overpayment, to Deposit Account No. 50-2207.

Respectfully submitted,

Date: 8-1-02

LeeAnn Gorthey
Registration No. 37,337

Correspondence Address:
Customer Number 22918
Phone: (650) 838-4403

Amendments to claims
U.S. Serial No. 09/754,468

1. (Amended) An antibacterial compound consisting of a substantially uncharged antisense oligomer containing from 10 [8] to 40 nucleotide subunits, each of said subunits comprising a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base, said base-pairing moieties [said oligomer] including a targeting nucleic acid sequence at least 10 nucleotides in length which is effective to hybridize to [(i) a bacterial tRNA sequence or (ii)] a target sequence, containing a translational start codon, within a bacterial nucleic acid which encodes [a] an E. coli *secA* protein [associated with cell division or the cell cycle,

said protein being selected from the group consisting of *zip*A, *sul*A, *secA*, *dic*A, *dic*B, *dic*C, *dic*F, *fts*A, *fts*I, *fts*N, *fts*K, *fts*L, *fts*Q, *fts*W, *fts*Z, *mur*C, *mur*D, *mur*E, *mur*F, *mur*G, *min*C, *min*D, *min*E, *mraY*, *mra*W, *mra*Z, *seq*A, and *ddl*B proteins, carbamate kinase, D-ala D-ala ligase, topoisomerase, alkyl hydroperoxide reductase, thioredoxin reductase, dihydrofolate reductase, and cell wall enzyme];

wherein[: each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence,]

adjacent subunits are joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate, phosphorodiamidate, carbonate, carbamate, amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and methylene-N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate,

and the ratio of uncharged linkages to charged linkages in the oligomer is at least 4:1.

6. (Amended) The compound of claim 1, wherein the [antisense oligomer has a length of from 15 to 20 subunits] targeting nucleic acid sequence has a length of 10 to 20 bases.

13. (Amended) The compound of claim [12] 1, wherein the targeting sequence has the sequence presented as SEQ ID NO: 47 (*E. coli sec*A).

17. (Amended) A method of treating a bacterial infection in a human or mammalian animal subject, comprising

administering to the subject, in a pharmaceutically effective amount, a substantially uncharged antisense oligomer containing from 10 [8] to 40 nucleotide subunits, each of said subunits comprising a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base, said base-pairing moieties including a targeting nucleic acid sequence at least 10 nucleotides in length which is effective to hybridize to [(i) a bacterial tRNA or (ii)] a target sequence, containing a translational start codon, within a bacterial nucleic acid which encodes [a] an *E. coli secA* protein [associated with cell division or the cell cycle,

said protein being selected from the group consisting of *zip*A, *sul*A, *secA*, *dic*A, *dic*B, *dic*C, *dic*F, *fts*A, *fts*I, *fts*N, *fts*K, *fts*L, *fts*Q, *fts*W, *fts*Z, *mur*C, *mur*D, *mur*E, *mur*F, *mur*G, *min*C, *min*D, *min*E, *mraY*, *mra*W, *mra*Z, *seq*A, and *ddl*B proteins, carbamate kinase, D-ala D-ala ligase, topoisomerase, alkyl hydroperoxide reductase, thioredoxin reductase, dihydrofolate reductase, and cell wall enzyme];

wherein[: each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence,]

adjacent subunits are joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate, phosphorodiamidate, carbonate, carbamate, amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and methylene-N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate,

and the ratio of uncharged linkages to charged linkages in the oligomer is at least 4:1.

23. (Amended) The method of claim 17, wherein the [antisense oligomer has a length of from 15 to 20 subunits] targeting nucleic acid sequence has a length of 10 to 20 bases.

30. The method of claim [29] 17, wherein the targeting sequence has the sequence presented as SEQ ID NO: 47.

36. (Amended) A livestock and poultry food composition containing a food grain supplemented with a subtherapeutic amount of an antibacterial compound, said compound consisting of a substantially uncharged antisense oligomer containing from 10 [8] to 40 nucleotide subunits, each of said subunits comprising a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base, said base-pairing moieties [said oligomer] including a targeting nucleic acid sequence at least 10 nucleotides in length which is effective to hybridize to [(i) a bacterial tRNA or (ii)] a target sequence, containing a translational start codon, within a bacterial nucleic acid which encodes [a] an *E. coli secA* protein [associated with cell division or cell wall synthesis,

said protein being selected from the group consisting of *zip*A, *sul*A, *secA*, *dic*A, *dic*B, *dic*C, *dic*F, *fts*A, *fts*I, *fts*N, *fts*K, *fts*L, *fts*Q, *fts*W, *fts*Z, *mur*C, *mur*D, *mur*E, *mur*F, *mur*G, *min*C, *min*D, *min*E, *mraY*, *mra*W, *mra*Z, *seq*A, and *ddl*B proteins, carbamate kinase, D-ala D-ala ligase, topoisomerase, alkyl hydroperoxide reductase, thioredoxin reductase, dihydrofolate reductase, and cell wall enzyme];

wherein[: each of said subunits comprises a 5- or 6-membered ring supporting a base-pairing moiety effective to bind by Watson-Crick base pairing to a respective nucleotide base in the bacterial nucleic acid sequence,]

adjacent subunits are joined by uncharged linkages selected from the group consisting of: uncharged phosphoramidate, phosphorodiamidate, carbonate, carbamate, amide, phosphotriester, alkyl phosphonate, siloxane, sulfone, sulfonamide, sulfamate, thioformacetyl, and methylene-N-methylhydroxylamino, or by charged linkages selected from the group consisting of phosphate, charged phosphoramidate and phosphorothioate,

and the ratio of uncharged linkages to charged linkages in the oligomer is at least 4:1.

39. (Amended) The composition of claim 36, wherein the [antisense oligomer has a length of from 15 to 20 nucleotide subunits] targeting nucleic acid sequence has a length of 10 to 20 bases.

40. (Amended) A method of preparing a vaccine against a selected bacteria, comprising:

incubating the bacteria in the presence of an antisense morpholino-based antisense oligomer having

(a) from 8 to 40 nucleotide subunits, including a targeting base sequence effective to hybridize to a translation initiation region in an mRNA transcribed from a *secA* gene of the selected bacteria[, selected from the group consisting of *zip*A, *sul*A, *secA*, *dic*A, *dic*B, *dic*C, *dic*F, *fts*A, *fts*I, *fts*N, *fts*K, *fts*L, *fts*Q, *fts*W, *fts*Z, *mur*C, *mur*D, *mur*E, *mur*F, *mur*G, *min*C, *min*D, *min*E, *mraY*, *mra*W, *mra*Z, *seq*A and *ddl*B]; and

(b) uncharged phosphorous-containing intersubunit linkages, as shown in Figures 2A-2D herein;

[im] in an amount of oligomer effective to produce replication-crippled, morphologically abnormal bacterial cells,

wherein the bacteria is *E coli*.

41. (Amended) A method of vaccinating a human or animal subject against a selected bacteria, comprising:

administering to the subject, replication-crippled, morphologically abnormal cells of the bacteria, prepared by incubating the bacteria in the presence of a morpholino-based antisense oligomer having

(a) from 8 to 40 nucleotide subunits, including a targeting base sequence effective to hybridize to a translation initiation region in an mRNA transcribed from a *secA* gene of the selected bacteria[, selected from the group consisting of *zip*A, *sul*A, *secA*, *dic*A, *dic*B, *dic*C, *dic*F, *fts*A, *fts*I, *fts*N, *fts*K, *fts*L, *fts*Q, *fts*W, *fts*Z, *mur*C, *mur*D, *mur*E, *mur*F, *mur*G, *min*C, *min*D, *min*E, *mraY*, *mra*W, *mra*Z, *seq*A and *ddl*B]; and

(b) uncharged phosphorous-containing chiral intersubunit linkages, as shown in Figures 2A-2D herein,

wherein the bacteria is *E coli*.